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EXAMINER

BROWN, STACY S

ART UNIT

PAPER NUMBER

1648

DATE MAILED: 06/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N .

09/914,036

Applicant(s)

KOEHL ET AL.

Examiner

Stacy S Brown

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 April 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>1</u> | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 1-8 and 11-16 is acknowledged.

Upon further consideration and in view of Applicant's persuasive arguments, the restriction requirement is withdrawn. Claims 1-18 are pending and examined.

Priority

2. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification and in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Specification

3. The use of trademarks has been noted in this application, particularly on pages 16-19. Trademarks should be capitalized or properly notated wherever they appear and be accompanied by the generic terminology. Applicant is requested to correct any other trademarks that have not been properly notated throughout the specification.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 and 11-16 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps. See MPEP § 2172.01. While all of the technical details of a method need not be recited, the claims should include enough information to clearly and accurately describe the invention and how it is to be practiced. The minimum requirements for method steps in a purification method should include a contacting step in which the crude viral preparation is contacted with the fluidized bed, a detection step in which the desired viral particles are adsorbed, and a correlation step in which the purification of viral particles is confirmed.

- Claim 4, the phrase "more particularly" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Further, claim 4 should recite proper Markush language, "selected from the group consisting of".
- Claim 7, "a central core comprising quartz and dextran chains covalently coupled to said agarose matrix" is unclear. Does Applicant mean "quartz or dextran"? Or are both quartz and dextran present at the same time? Clarification is requested.
- Claim 8 and dependent claims 15 and 16, "comprising carrying out under conductivity conditions" is unclear. What specifically is being carried out under conductivity conditions - the adsorption step or the entire purification? Clarification is requested.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 9-11 and 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Shabram (WO96/27677). The claims are drawn to a method of purifying a crude viral preparation containing viral particles of interest, comprising at least one fluidized-bed adsorption step. The viral particles of interest can be recombinant adenoviral particles. Also claimed is a method of producing viral particles comprising infection/transfection of a cell line with a viral vector, culturing the infected cell line and purifying the viral preparation with at least one fluidized-bed adsorption step.

Shabram discloses a method for purifying recombinant viral particles from a cell lysate comprising two chromatography steps (fluidized-bed adsorption), see abstract, page 8, lines 4-8 and page 9, lines 13-15. Shabram teaches that adenovirus vectors can be purified in the method (page 3, lines 1-2). Therefore, claims 1, 9-11 and 17-18 are anticipated by Shabram.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2-8 and 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shabram (WO96/27677) as applied to claims 1, 9-11 and 17-18 above, and further in view of Hjorth (*Trends in Biotech.*, 1997, 15:230-235) and Shabram *et al* (5,837,520). The claims are drawn to particulars of the fluidized bed, wherein the fluidized bed comprising particles suspended in fluid under the action of one or more forces selected from the group consisting of mechanical, electromagnetic, magnetic, gravitational and electrical forces. There is a phase for expanding the adsorbent particle in a chromatography column by applying an ascending flow of buffer, a phase for loading the crude viral preparation in the lower part of the column, a phase for washing, sedimentation, and elution by applying a descending flow of buffer. The particles can be polymers that bear at least one ligand that binds specifically and reversibly to an antiligand (viral particle). The ligand has a positively charged group. The adsorbent is comprised of an agarose matrix and central core comprising quartz and dextran chains covalently coupled to the matrix, on which is attached the positively charged group. The positively charged group can be DMAE, DEAE, TMAE, Q group, the guanidinium group or the imine group (PEI).

The teachings of Shabram (WO/96) are above. Shabram fails to teach the particulars of the fluidized bed. However, Hjorth teaches expanded-bed adsorption and fluidized-bed adsorption. In expanded-bed adsorption, the adsorbent particles are suspended in fluid in a column (page 230, second column) which allow cells and cell debris to pass through. Some of the adsorbents useful in expanded-bed adsorption are listed in Table 1, page 232, and include agarose-quartz to which is attached a DEAE ligand. The steps in the process include expansion (upward flow), application, washing, settling and elution in downward flow.

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Shabram (WO/96) fails to teach the particulars of the positively charged group.

However, Shabram *et al* ('520) teaches the purification of adenoviral vectors in columns, using Resource Q anion exchange column (col. 3, lines 34-36), and other positively charged organic moieties covalently cross-linked to an inert polymeric support. The organic moieties include TMAE, DEAE, DMAE and PEI (col. 5, lines 1-3).

It would have been obvious to incorporate the particulars of the fluidized bed and positively charged groups into the method of Shabram (WO/96). One would have been motivated to use the adsorbent particles and matrices in the fluidized bed adsorption because Hjorth and Shabram ('520) use the same method of expanded/fluidized bed adsorption. The features taught by Hjorth and Shabram ('520) are commonly used in fluidized/expanded bed adsorption. One would have had a reasonable expectation of success that the adsorbent particles and matrices of Hjorth and Shabram ('520) would have worked in the method of Shabram because

Shabram discloses a method for purifying recombinant viral particles from a cell lysate comprising two chromatography steps (fluidized-bed adsorption), see abstract, page 8, lines 4-8 and page 9, lines 13-15. Regarding the conductivity conditions, one of ordinary skill in the art would have known how to run the column given the well known art of chromatography. Lacking any evidence to the contrary, the conductivity conditions commonly used in other fluidized-bed adsorption columns are expected to work in the method of Shabram (WO/96) in combination with Hjorth and Shabram ('520).

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

7. No claim is allowed.

Papers relating to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 located in Crystal Mall 1. The Fax number for Art Unit 1648 is (703) 308-4426. All Group 1600 Fax machines will be available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Stacy S. Brown, whose telephone number is (703) 308-2361. The Examiner can normally be reached on Monday through Friday from 6:30 AM-4:00 PM, (EST). If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, James C. Housel, can be reached at (703) 308-4027. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SSB

Stacy S. Brown
June 6, 2003

James C. Housel
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